Jan DeLaval

Access DB# 47948

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Josephine Young Examiner #: 79813 Date: 10-25-02

Art Unit: 1623 Phone Number 30 605-1201 Serial Number: 09/991,978

Mail Box and Bldg/Room Location: CM1 9D04 Results Format Preferred (circle): PAPER DISK E-MAIL

CM1 8B19 (after 11/05: 8D04)

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Excipients containing low residual solvent and method for producing the same

Inventors (please provide full names): HUANG, Yun-Peng; LEE, Fangchan (or Fangchen); SHAW, Jer-Yen

Earliest Priority Filing Date: 10-19-2001

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Attached: 1) Current Claims; 2) Bib Sheet; 3) Assignment Info

Please search: 1) claim 1 – pt. of novelty: residual solvent less than 3000 ppm

2) claim 13: [redacted] pt. of novelty: methods of drying excipient to remove solvent

3) claim 8: pt. of novelty: excipients w/ water absorbing radical, such as an acetate linked to the polysaccharide (see also claims 9-11)

Thanks!

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher: AM	NA Sequence (#)		STN	✓
Searcher Phone #: 4458	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)		Questel/Orbit	
Date Searcher Picked Up: 10/29/02	Bibliographic	✓	Dr.Link	
Date Completed: 10/29/02	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:	Fulltext		Sequence Systems	
Clerical Prep Time: 15	Patent Family		WWW/Internet	
Online Time: + 195	Other		Other (specify)	

PTO-1590 (8-01)

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FILE COVERS 1907 - 29 Oct 2002 VOL 137 ISS 18
FILE LAST UPDATED: 28 Oct 2002 (20021028/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d all hitstr tot

L104 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2002 ACS
AN **2002:184878** HCAPLUS
DN **136:236851**
TI Pharmaceutical modified release formulation
IN Eklund, Marianne; Lofroth, Jan-Erik; Skantze, Urban
PA Astrazeneca AB, Swed.; Astrazeneca UK Limited
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-20
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002019990	A1	20020314	WO 2001-GB3861	20010830
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001084189	A5	20020322	AU 2001-84189	20010830
PRAI	SE 2000-3125	A	20000905		
	WO 2001-GB3861	W	20010830		

AB A pharmaceutical modified release formulation comprising a pharmacol. active substance and a modified **water**-sol. **polysaccharide**, which modified **water**-sol. **polysaccharide** is obtainable by forming a ppt. of a **water**-sol. **polysaccharide** by contacting a soln. of the **water**

-sol. **polysaccharide** with a **solvent** in which the **polysaccharide** is poorly sol. or insol. or milling a **water**-sol. **polysaccharide**. The modified **water**-sol. **polysaccharides** provide modified release formulations with high tablet hardness. Also claimed are a process for prepg. the modified release formulation, and the use of the modified **water**-sol. **polysaccharides** as an **excipient** in a pharmaceutical formulation. Thus, an aq. 1% soln. of hydroxyethyl **cellulose** was poured into **acetone**. The final ratio of **acetone**/**water** was 3:1. The **cellulose** deriv. after drying was stored in a closed container. Tablets were obtained from the above **cellulose** 58, fluvastatin 10, and Mg stearate 0.7 mg. In 12 h, 30% drug was released.

ST pharmaceutical modified release **polysaccharide**

IT Granulation
Hardness (mechanical)
Milling (size reduction)
(pharmaceutical modified release formulation)

IT Alcohols, uses
Aromatic hydrocarbons, uses
Carboxylic acids, uses
Esters, uses
Ethers, uses
Hydrocarbons, uses
Ketones, uses
Nitriles, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)
(pharmaceutical modified release formulation)

IT **Polysaccharides, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical modified release formulation)

IT Drug delivery systems
(sustained-release; pharmaceutical modified release formulation)

IT Drug delivery systems
(tablets; pharmaceutical modified release formulation)

IT **64-17-5, Ethanol**, uses 64-18-6, Formic acid, uses **64-19-7**, Acetic acid, uses **67-56-1, Methanol**, uses **67-63-0, Isopropanol**, uses **67-64-1, Acetone**, uses 67-68-5, DMSO, uses 97-64-3, Ethyl lactate 108-88-3, Toluene, uses 110-54-3, Hexane, uses 119-36-8, Methyl salicylate 123-39-7, Methylformamide 141-78-6, EtOAc, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)
(pharmaceutical modified release formulation)

IT **9000-30-0, Guar gum** 9000-40-2, Locust bean gum 9000-65-1, Tragacanth gum 9004-62-0, Hydroxyethyl **cellulose** 51384-51-1, Metoprolol 56392-17-7, Metoprolol tartrate 72509-76-3, Felodipine 93957-54-1, Fluvastatin 93957-55-2, Fluvastatin sodium 98418-47-4, Metoprolol succinate 192939-46-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical modified release formulation)

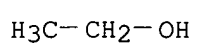
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

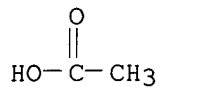
(1) Cibus Pharmaceutical; WO 9616638 A 1996 HCAPLUS
(2) Cibus Pharmaceutical; WO 9616639 A 1996 HCAPLUS
(3) Cibus Pharmaceutical; WO 9640163 A 1996 HCAPLUS
(4) Fmc Corporation; WO 9415643 A 1994 HCAPLUS

IT **64-17-5, Ethanol**, uses **64-19-7**, Acetic acid, uses **67-56-1, Methanol**, uses **67-63-0, Isopropanol**, uses **67-64-1, Acetone**, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)

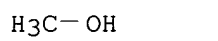
(pharmaceutical modified release formulation)
RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)



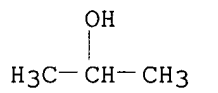
RN 64-19-7 HCAPLUS
CN Acetic acid (7CI, 8CI, 9CI) (CA INDEX NAME)



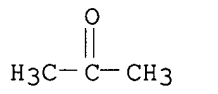
RN 67-56-1 HCAPLUS
CN Methanol (8CI, 9CI) (CA INDEX NAME)



RN 67-63-0 HCAPLUS
CN 2-Propanol (9CI) (CA INDEX NAME)



RN 67-64-1 HCAPLUS
CN 2-Propanone (9CI) (CA INDEX NAME)



IT **9000-30-0, Guar gum**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical modified release formulation)
RN 9000-30-0 HCAPLUS
CN Guar gum (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L104 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2002 ACS
AN **2002:123500** HCAPLUS
DN **136:189437**
TI Preserving compositions for contact lenses containing **chitosan** derivatives
IN Hung, William M.; Bergbauer, Katrina L.; Su, Kai C.; Wang, Guigui
PA USA
SO U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 611,160.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61L012-08
NCL 422028000

CC **63-8** (Pharmaceuticals)
Section cross-reference(s): 10

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002018732	A1	20020214	US 2001-838528	20010419
PRAI	US 2000-199406P	P	20000421		
	US 2000-202548P	P	20000510		
	US 2000-611160	A2	20000706		

OS MARPAT 136:189437

AB The present invention is directed to a pharmaceutical preserving compn. comprising: (a) at least one **chitosan** or **chitosan** deriv. and (b) at least one buffer soln., as well as methods of preserving contact lens solns. and disinfecting contact lens using such compn. The present invention is further directed to a method of prepg. O-acetylated **chitosan** or **chitosan** derivs. comprising the steps of dissolving the **chitosan** or **chitosan** deriv. into an aq. acidic soln. and reacting the **chitosan** or **chitosan** deriv. with an acetylating agent in the presence of a phase transfer reagent. For example, a soln. was prepd. contg. glycol **chitosan** 0.5%, Pluronic F 68 0.05%, EDTA 0.05%, sodium borate decahydrate 0.08%, boric acid 0.72%, water up to 100.00 mL, 0.5% **NaOH** soln. as needed for pH of 6.6, 7.2 or 7.8, and NaCl to obtain 300.+-.10 mOsm. The pH 6.6 and 7.2 formulations of glycol **chitosan** were more effective in killing Pseudomonas aeruginosa in 24 h than the glycol **chitosan** formulation at pH = 7.8.

ST **chitosan** buffer soln preservation contact lens disinfection

IT Aspergillus niger
Candida albicans
Escherichia coli
Pseudomonas aeruginosa
Staphylococcus aureus
(inhibition of; preserving compns. for contact lenses contg. **chitosan** derivs. and buffers)

IT Acetylation
Phase transfer catalysts
(prepn. of sol. **chitosan** derivs. for preserving compns. for contact lenses)

IT Antimicrobial agents
Biocides
Buffers
Contact lenses
Disinfectants
Preservation
Sterilization and Disinfection
Surfactants
(preserving compns. for contact lenses contg. **chitosan** derivs. and buffers)

IT Bases, biological studies
Crown ethers
Phosphonium compounds
Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preserving compns. for contact lenses contg. **chitosan** derivs. and buffers)

IT Pyridinium compounds
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salts; preserving compns. for contact lenses contg. **chitosan** derivs. and buffers)

IT Drug delivery systems
(solns.; preserving compns. for contact lenses contg. **chitosan** derivs. and buffers)

IT 77-86-1, Tris (buffer) 77-92-9, biological studies 11129-12-7, Borate

14265-44-2, Phosphate, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(buffer; preserving compns. for contact lenses contg. **chitosan** derivs. and buffers)

IT 60-00-4, EDTA, biological studies 139-33-3, Disodium EDTA
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preserving compns. for contact lenses contg. **chitosan** derivs. and buffers)

IT **9012-76-4D, Chitosan,** derivs.
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preserving compns. for contact lenses contg. **chitosan** derivs. and buffers)

IT 42617-20-9P, **Chitosan** acetate (ester)
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preserving compns. for contact lenses contg. **chitosan** derivs. and buffers)

IT 56-37-1, Benzyltriethylammonium chloride **64-19-7**, Acetic acid, biological studies **67-56-1, Methanol**, biological studies 75-57-0, Tetramethylammonium chloride 104-74-5, 1-Dodecylpyridinium chloride 108-24-7, Acetic anhydride 140-72-7, 1-Cetylpyridinium bromide 311-28-4, Tetrabutylammonium iodide 1310-58-3, Potassium hydroxide, biological studies 1330-43-4, Sodium borate 1643-19-2, Tetrabutylammonium bromide 3115-68-2, Tetrabutylphosphonium bromide 5574-97-0, Tetrabutylammonium dihydrogen phosphate 7647-14-5, Sodium chloride, biological studies **9012-76-4, Chitosan** 14187-32-7, Dibenzo-18-crown-6 14937-45-2, Hexadecyltributylphosphonium bromide 15128-65-1 17455-13-9, 18-Crown-6 33100-27-5, 15-Crown-5 39280-86-9, Glycol **chitosan** 60039-27-2 83512-85-0, Carboxymethyl **chitosan** 84069-44-3, Hydroxypropyl **chitosan** 92091-35-5 106392-12-5, Pluronic F 68 398139-87-2 398452-94-3, Dihydroxybutyl **chitosan**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preserving compns. for contact lenses contg. **chitosan** derivs. and buffers)

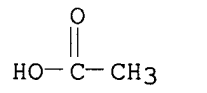
IT **9012-76-4D, Chitosan,** derivs.
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preserving compns. for contact lenses contg. **chitosan** derivs. and buffers)

RN 9012-76-4 HCAPLUS
CN Chitosan (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **64-19-7**, Acetic acid, biological studies **67-56-1, Methanol**, biological studies **9012-76-4, Chitosan**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preserving compns. for contact lenses contg. **chitosan** derivs. and buffers)

RN 64-19-7 HCAPLUS
CN Acetic acid (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 67-56-1 HCAPLUS
CN Methanol (8CI, 9CI) (CA INDEX NAME)

H_3C-OH

RN 9012-76-4 HCAPLUS
CN Chitosan (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L104 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2002 ACS
AN **2000:371824** HCAPLUS
DN **132:339320**
TI Extraction of **polysaccharide** from Ledebouriella divaricata for therapeutic use
IN Niu, Jianzhao; Lu, Yunru; Zhang, Guiyan; Zhou, Yong; Li, Yungu; Long, Zhixian
PA Beijing Chinese Medicine Univ., Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
IC ICM A61K035-78
ICS A61K009-08
CC **63-4** (Pharmaceuticals)
Section cross-reference(s): **1**, 11
FAN.CNT 1

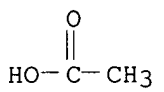
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1135900	A	19961120	CN 1995-104920	19950510
CN 1065751	B	20010516		

AB The title method comprises raw material smashing, degreasing with lower alc. (**methanol**, ethanol, or propanol), extg. three time with boiling or alk. water (raw material: alkali water= 1 : 6-12) for 0.5-2 h, neutralizing the exts. with acid, concg. to dense slurry, centrifugating at 3000 rpm for 10-20 min to obtain supernatant, mixing with lower alc., cooling and setting for 8 h, siphoning to discharge supernatant, centrifugating and drying sediment, dissolving the dried sediments in hot water, filtering to remove insol. matter, dialyzing, ultrafiltrating (.ltoreq. 60 000), concg. at .ltoreq.60.degree., adding lower alc. up to 80-85% to ppt. **polysaccharide**, cooling, sepg. sediments by centrifugation, and drying to obtain a final product. The alkali includes monovalent metal hydroxide, carbonate, acetate, and ammonium hydroxide. Acid used for neutralizing pH includes 36% acetic acid and glacial acetic acid. The **polysaccharide** is made into injection [2-10 mg/mL, pH 7.5-9] by heating, dissolving, filtrating, cooling, filtrating, bottling and sterilizing. The **polysaccharide** showed immunostimulant, anti-tumor, and anti-AIDS activities.
ST Ledebouriella **polysaccharide** immunostimulant antitumor AIDS
IT Anti-AIDS agents
Antitumor agents
Immunostimulants
Saposhnikovia divaricata
(extn. of **polysaccharide** from Ledebouriella divaricata for therapeutic use)
IT **Polysaccharides, biological studies**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(extn. of **polysaccharide** from Ledebouriella divaricata for therapeutic use)
IT Drug delivery systems
(injections; extn. of **polysaccharide** from Ledebouriella divaricata for therapeutic use)

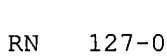
IT 64-17-5, Ethanol, uses **64-19-7**, Acetic acid, uses **67-56-1**, **Methanol**, uses 71-23-8, Propanol, uses **127-09-3**, Sodium acetate **1310-73-2**, **Sodium hydroxide**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(extn. of **polysaccharide** from Ledebouriella for therapeutic use)

IT **64-19-7**, Acetic acid, uses **67-56-1**, **Methanol**, uses **127-09-3**, Sodium acetate **1310-73-2**, **Sodium hydroxide**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(extn. of **polysaccharide** from Ledebouriella for therapeutic use)

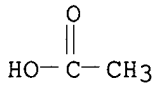
RN 64-19-7 HCAPLUS
CN Acetic acid (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 67-56-1 HCAPLUS
CN Methanol (8CI, 9CI) (CA INDEX NAME)



RN 127-09-3 HCAPLUS
CN Acetic acid, sodium salt (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 1310-73-2 HCAPLUS
CN Sodium hydroxide (Na(OH)) (9CI) (CA INDEX NAME)

L104 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2002 ACS
AN **1998:586342** HCAPLUS
DN **129:204387**
TI Manufacture of acylated **chitin** or **chitosan** and fibers, films, foams, or other moldings made of the products
IN Yoshikawa, Masatoshi; Okumura, Tadashi
PA Omikenshi K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C08B037-08
ICS A61L027-00; C08J005-18; C08L001-24; C08L005-08

CC 44-5 (Industrial Carbohydrates)
Section cross-reference(s): 40, **63**

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 10237106	A2	19980908	JP 1997-54070	19970220

AB Title products as aq. **NaOH** solns. are manufd. by dissolving **chitosan** or partially deacetylated **chitin** in mixts. of AcOH and **MeOH** and adding acid anhydrides to the solns., optionally assocd. with heating, for acylation followed by reaction with .gtoreq.30% aq. **NaOH** at a temp. lower than room temp. and by addn. of ice for dissolving. The solns. themselves or mixts. with **cellulose** viscose are converted into fibers, films, foams, or other moldings, which are used as medical goods, sanitary goods, wearing apparel, etc. Thus, dissolving 0.16 g **chitosan** in 10% aq. AcOH to give 4% soln., dilg. of the soln. with **MeOH** to give a 20% soln., adding of 2 mol (based on hexamine) propionic anhydride to the soln., crushing of the resulted gel, dialyzing of the crushed gel, swelling of the crushed gel by 46% aq. **NaOH** at room temp. for 2 h, and adding crushed ice to the gel gave 1% soln. of **NaOH** concn. 14%. Then, swelling of the 2.0 of the gel in 46% aq. **NaOH** to give 10% soln., cooling of the soln. in refrigerator for 1 day, adding crushed ice to the soln., spinning of the soln. followed by refining gave 4.71-denier fiber having tenacity 0.52 g/denier and elongation 25.9%.

ST acylation **chitin chitosan** fiber manuf; aq **sodium hydroxide** soln acylated **chitin**; medical good acylated **chitin chitosan**; sanitary good acylate **chitin chitosan**; **cellulose** viscose **chitosan chitin** molding; propionic anhydride **chitin chitosan** acylation

IT Rayon, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(acylation of chiton or **chitosan** for prepn. of aq. **sodium hydroxide** solns. for fibers contg.)

IT Clothing
Foams
Medical goods
(acylation of chiton or **chitosan** for prepn. of aq. **sodium hydroxide** solns. for medical goods)

IT Viscose
(acylation of chiton or **chitosan** for prepn. of aq. **sodium hydroxide** solns. for moldings contg.)

IT Synthetic polymeric fibers, preparation
RL: IMF (Industrial manufacture); PREP (Preparation)
(**chitosan** propionate; acylation of chiton or **chitosan** for prepn. of aq. **sodium hydroxide** solns. for molding)

IT **1398-61-4DP, Chitin**, partially deacetylated, acylated
124384-94-7P, **Chitosan** butyrate
RL: IMF (Industrial manufacture); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(acylation of chiton or **chitosan** for prepn. of aq. **sodium hydroxide** solns. for molding)

IT **1310-73-2, Sodium hydroxide**, uses
RL: TEM (Technical or engineered material use); USES (Uses)
(aq.; in acylation of chiton or **chitosan** for prepn. of aq. **sodium hydroxide** solns. for moldings)

IT 84563-57-5P, **Chitosan** propionate
RL: IMF (Industrial manufacture); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(fiber; acylation of chiton or **chitosan** for prepn. of aq. **sodium hydroxide** solns. for molding)

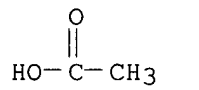
IT **64-19-7**, Acetic acid, uses **67-56-1, Methanol**,

uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvents; acylation of chiton or **chitosan** for prepn. of aq. **sodium hydroxide** solns. for moldings)
IT **1398-61-4DP, Chitin**, partially deacetylated, acylated
RL: IMF (Industrial manufacture); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(acylation of chiton or **chitosan** for prepn. of aq. **sodium hydroxide** solns. for molding)
RN 1398-61-4 HCAPLUS
CN Chitin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **1310-73-2, Sodium hydroxide**, uses
RL: TEM (Technical or engineered material use); USES (Uses)
(aq.; in acylation of chiton or **chitosan** for prepn. of aq. **sodium hydroxide** solns. for moldings)
RN 1310-73-2 HCAPLUS
CN Sodium hydroxide (Na(OH)) (9CI) (CA INDEX NAME)

Na—OH

IT **64-19-7**, Acetic acid, uses **67-56-1, Methanol**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvents; acylation of chiton or **chitosan** for prepn. of aq. **sodium hydroxide** solns. for moldings)
RN 64-19-7 HCAPLUS
CN Acetic acid (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 67-56-1 HCAPLUS
CN Methanol (8CI, 9CI) (CA INDEX NAME)

L104 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2002 ACS
AN **1997:594625** HCAPLUS
DN **127:253189**
TI Use of microcrystalline **starch** products as tableting **excipient**
IN Buwalda, Pieter Lykle; Arends-Scholte, Anna Willemina
PA Cooperatieve Verkoop- en Productievereniging van Aardappelmeel en Derivaten, Neth.; Buwalda, Pieter Lykle; Arends-Scholte, Anna Willemina
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA Dutch
IC ICM A61K009-20
ICS C08B030-12; C12P019-14
CC 63-6 (Pharmaceuticals)
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 9731627	A1	19970904	WO 1997-NL97	19970228
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	NL 1002493	C2	19970901	NL 1996-1002493	19960229
	AU 9722353	A1	19970916	AU 1997-22353	19970228
PRAI	NL 1996-1002493		19960229		
	WO 1997-NL97		19970228		

AB The use of a microcryst. **starch** as tableting **excipient**, wherein the microcryst. **starch** used is obtainable by the action of an acid and/or enzyme on granular **starch**, preferably a cereal **starch**, in an aq. suspension, dehydration by means of a **water**-miscible org. **solvent** and drying the dehydrated **starch** product. The microcryst. **starch** preferably has a sp. surface area of at least 1 m2/g. Thus, 450 g of an aq. suspension of corn **starch** was heated with 28 mL 6N HCl for 24 h at 54.degree., after cooling down it was sepd., treated with NaOH soln., and washed with **water**. A sample of 100 g of the wet **starch** product was suspended in 800 **ethanol** and stirred for 30 min, then was sepd. by filtration and dried in the air. Tablets made by direct compression of the microcryst. **starch** had sp. surface area of 1.1 m2/g and disintegration time of 4 min.

ST microcryst **starch** pharmaceutical tablet **excipient**

IT **Solvents**
(org.; use of microcryst. **starch** products as tableting **excipient**)

IT Drug delivery systems
(tablets, compressed; use of microcryst. **starch** products as tableting **excipient**)

IT Drug delivery systems
(tablets; use of microcryst. **starch** products as tableting **excipient**)

IT Enzymes, uses
RL: CAT (Catalyst use); USES (Uses)
(use of microcryst. **starch** products as tableting **excipient**)

IT Acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(use of microcryst. **starch** products as tableting **excipient**)

IT **9005-25-8, Starch**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst.; use of microcryst. **starch** products as tableting **excipient**)

IT 9000-90-2, .alpha.-Amylase
RL: CAT (Catalyst use); USES (Uses)
(use of microcryst. **starch** products as tableting **excipient**)

IT 7647-01-0, Hydrochloric acid, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(use of microcryst. **starch** products as tableting **excipient**)

IT **9005-25-8, Starch**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst.; use of microcryst. **starch** products as tableting **excipient**)

RN 9005-25-8 HCAPLUS

CN Starch (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L104 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2002 ACS
AN **1996:365810** HCAPLUS
DN **125:19078**
TI **Starch** products as tabletting **excipients**, method for preparing same, and method for making tablets
IN Arends-Scholte, Anna Willemina; Bergsma, Jacob; Eissens, Anko Cornelus; Gotlieb, Kornelis Fester; Lerk, Coenraad Ferdinand; Swinkels, Josephus Johannes Maria; Te Wierik, Gerrit Henk Peter
PA Cooperatieve Verkoop-en Productievereniging van Aardappelmeel en, Neth.
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-20
ICS C12P019-14; C08B030-12
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9609815	A1	19960404	WO 1995-NL321	19950925
	W: AU, BR, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, PL, SK, US, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	NL 9401572	A	19960501	NL 1994-1572	19940927
	TW 397691	B	20000711	TW 1995-84109805	19950919
	AU 9536881	A1	19960419	AU 1995-36881	19950925
	EP 783300	A1	19970716	EP 1995-934331	19950925
	EP 783300	B1	19981202		
	R: CH, DE, FR, GB, LI, NL				
	JP 10506627	T2	19980630	JP 1995-511635	19950925
	US 6010717	A	20000104	US 1997-809904	19970324
PRAI	NL 1994-1572	A	19940927		
	WO 1995-NL321	W	19950925		

AB The invention relates to a tabletting **excipient** based on disintegrated **starch** granules, which is characterized by a content of long-chain **amylose** of at least 10% by wt. based on the dry substance, a cold **water**-soly. of at most 25% by wt. and a specific area of at least 1 m2/g. The invention further relates to a method for prepg. such tabletting **excipient** and to the use of the tabletting **excipient** in tablets. The method for prepg. such tabletting **excipient** is characterized in that an aq. soln. of gelatinized **amylose**- and **amylopectin**-contg. **starch** is treated with a debranching enzyme and an .alpha.-amylase, and the obtained hydrated **starch** product is dehydrated by means of freeze-drying or by means of a **water**-miscible org. **solvent** and subsequent drying. Or, gelatinized **starch** is maintained in contact with an aq. soln. of a salting-gout salt, the obtained hydrated cold **water**-insol. **starch** product is isolated from the salt soln. and the isolated **starch** product is dehydrated by means of freeze-drying or by means of a **water**-miscible org. **solvent** with subsequent drying.

ST **starch** product tabletting **excipient** pharmaceutical
IT Pharmaceutical dosage forms
(controlled-release, **starch** products as tabletting **excipients**, method for prepg. same, and method for making tablets)
IT Enzymes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(debranching, **starch** products as tabletting **excipients**, method for prepg. same, and method for making tablets)

IT Pharmaceutical dosage forms
(tablets, **starch** products as tabletting **excipients**, method for prepg. same, and method for making tablets)

IT 9000-90-2, .alpha.-Amylase 9075-68-7, Promozyme 200L
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**starch** products as tabletting **excipients**, method for prepg. same, and method for making tablets)

IT **9005-82-7, Amylose**
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(**starch** products as tabletting **excipients**, method for prepg. same, and method for making tablets)

IT **64-17-5, Ethanol**, uses 10034-99-8, Magnesium sulfate heptahydrate
RL: NUU (Other use, unclassified); USES (Uses)
(**starch** products as tabletting **excipients**, method for prepg. same, and method for making tablets)

IT 58-55-9, Theophylline, biological studies 557-04-0, Magnesium stearate 152442-43-8, Paselli WA4
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**starch** products as tabletting **excipients**, method for prepg. same, and method for making tablets)

IT **9005-25-8DP, Starch**, partial hydrolysis products
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**starch** products as tabletting **excipients**, method for prepg. same, and method for making tablets)

IT **9005-82-7, Amylose**
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(**starch** products as tabletting **excipients**, method for prepg. same, and method for making tablets)

RN 9005-82-7 HCAPLUS
CN Amylose (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **64-17-5, Ethanol**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(**starch** products as tabletting **excipients**, method for prepg. same, and method for making tablets)

RN 64-17-5 HCAPLUS
CN Ethanol (9CI) (CA INDEX NAME)

H_3C-CH_2-OH

IT **9005-25-8DP, Starch**, partial hydrolysis products
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**starch** products as tabletting **excipients**, method for prepg. same, and method for making tablets)

RN 9005-25-8 HCAPLUS
CN Starch (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L104 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2002 ACS
AN **1995:436053** HCAPLUS
DN **122:197030**
TI Large intestine-disintegrable compositions containing **cellulose** and **water**-soluble **chitosan** and preparation of the **water**-soluble **chitosan**
IN Hagino, Yoshinori; Terabe, Akira; Matsumoto, Takayuki
PA Aicello Chemical Co, Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K047-38
ICS A61K047-36
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 33
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 07002701	A2	19950106	JP 1993-170982	19930617
JP 2521229	B2	19960807		

AB Compns., those pass through the small intestine and disintegrate in the large intestine, contain fine **cellulose** and 20-200 wt.% (based on fine **cellulose**) **water**-sol. **chitosan** (deacetylation degree 40-60 mol%). The **water**-sol. **chitosan** is prepd. by addn. of Ac2O **dild.** with alcs. to acid solns. contg. **chitosan** (deacetylation degree .gtoreq.95 mol%) for N-acetylation of the **chitosan** to deacetylation degree 40-60 mol%. **Chitosan** (wt.-av. mol. wt. 63,000, deacetylation degree 99 mol%) was dissolved in aq. 5 wt.% AcOH soln., the soln. was mixed with **MeOH**, Ac2O **dild.** with **MeOH** was then added dropwise to the soln., and stirred at room temp. for 3 h to give **water**-sol. **chitosan** (deacetylation degree 52%). Tablets contg. vitamin A was coated with a mixt. of 90 g aq. soln. contg. 4% the **water**-sol. **chitosan** and 60 g dispersion contg. 12.5% fine **cellulose** to give coated tablets, which did not disintegrate at pH .gtoreq.6.5 and disintegrated at pH .ltoreq.6. The tablets disintegrated and released vitamin A in the presence of Bacteroides vulgatus in cysteine-thioglycolic acid-contg. physiol. NaCl soln.

ST large intestine disintegrable pharmaceutical **cellulose**; acetylation **chitosan** acetic anhydride; **water** sol **chitosan** prepn pharmaceutical; enteric coated tablet **cellulose chitosan**

IT Acetylation
(N-, of **chitosan**; large intestine-disintegrable pharmaceutical compns. contg. fine **cellulose** and **water**-sol. **chitosan**)

IT Acids, uses
Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(in **chitosan** N-acetylation with acetic anhydride; large intestine-disintegrable pharmaceutical compns. contg. fine **cellulose** and **water**-sol. **chitosan**)

IT Intestine
(large, large intestine-disintegrable pharmaceutical compns. contg. fine **cellulose** and **water**-sol. **chitosan**)

IT Pharmaceutical dosage forms
(tablets, enteric-coated, large intestine-disintegrable pharmaceutical compns. contg. fine **cellulose** and **water**-sol. **chitosan**)

IT **9012-76-4, Chitosan**

RL: RCT (Reactant); RACT (Reactant or reagent)
(N-acetylation of; large intestine-disintegrable pharmaceutical compns. contg. fine **cellulose** and **water**-sol. **chitosan**)

IT 108-24-7, Acetic anhydride
RL: RCT (Reactant); RACT (Reactant or reagent)
(**chitosan** N-acetylation with; large intestine-disintegrable pharmaceutical compns. contg. fine **cellulose** and **water**-sol. **chitosan**)

IT **64-19-7**, Acetic acid, uses **67-56-1**, **Methanol**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(in **chitosan** N-acetylation with acetic anhydride; large intestine-disintegrable pharmaceutical compns. contg. fine **cellulose** and **water**-sol. **chitosan**)

IT **9012-76-4DP**, **Chitosan**, partially N-acetylated
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(large intestine-disintegrable pharmaceutical compns. contg. fine **cellulose** and **water**-sol. **chitosan**)

IT **9004-34-6**, **Cellulose**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(large intestine-disintegrable pharmaceutical compns. contg. fine **cellulose** and **water**-sol. **chitosan**)

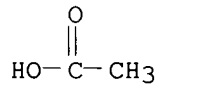
IT **9012-76-4**, **Chitosan**
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-acetylation of; large intestine-disintegrable pharmaceutical compns. contg. fine **cellulose** and **water**-sol. **chitosan**)

RN 9012-76-4 HCAPLUS
CN Chitosan (8CI, 9CI) (CA INDEX NAME)

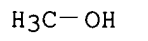
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **64-19-7**, Acetic acid, uses **67-56-1**, **Methanol**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(in **chitosan** N-acetylation with acetic anhydride; large intestine-disintegrable pharmaceutical compns. contg. fine **cellulose** and **water**-sol. **chitosan**)

RN 64-19-7 HCAPLUS
CN Acetic acid (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 67-56-1 HCAPLUS
CN Methanol (8CI, 9CI) (CA INDEX NAME)



IT **9012-76-4DP**, **Chitosan**, partially N-acetylated
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(large intestine-disintegrable pharmaceutical compns. contg. fine **cellulose** and **water**-sol. **chitosan**)

RN 9012-76-4 HCAPLUS
CN Chitosan (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9004-34-6, Cellulose**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(large intestine-disintegrable pharmaceutical compns. contg. fine **cellulose** and **water**-sol. **chitosan**)
RN 9004-34-6 HCAPLUS
CN Cellulose (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

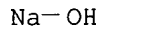
L104 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2002 ACS
AN **1991:230257** HCAPLUS
DN **114:230257**
TI Sorption and diffusion of water and alcohols in **chitosan** complex membranes
AU Baek, Jin Woo; Shin, Eun Mi; Lee, Young Moo
CS Coll. Eng., Hanyang Univ., Seoul, 133-791, S. Korea
SO Polymer (Korea) (1990), 14(3), 273-81
CODEN: POLLDG; ISSN: 0379-153X
DT Journal
LA English
CC 38-3 (Plastics Fabrication and Uses)
Section cross-reference(s): **33**, 37
AB The sorption and diffusion of water and alc. (**MeOH**, EtOH, iso-PrOH, and PrOH) in **chitosan**-AcOH complex membranes and **chitosan**-metal ion complex membranes were studied. From the plots of absorption of solvents as a function of square root of time, diffusion coeffs. (D) were calcd. As an alkali treating time was prolonged, membrane became more cryst. and thus an equil. sorption value decrease. The decrease equil. sorption and D of lower alcs. were in the order of **MeOH**, EtOH, iso-PrOH, and PrOH resulting from their increased molar volume and decreased heat of vaporization.
ST **chitosan** complex membrane sorption diffusion; acetic acid **chitosan** complex membrane; metal **chitosan** complex membrane; water sorption diffusion **chitosan** membrane; alc sorption diffusion **chitosan** membrane; alkali treatment **chitosan** membrane transport
IT Membranes
(from **chitosan** complexes with acetic acid or with metal ions, sorption and diffusion of water and alcs. in, alkali treatment effect on)
IT Sorption
(of water and alcs., in **chitosan** complex membranes, alkali treatment effect on)
IT Diffusion
(of water and alcs., in **chitosan** complex membranes, effect of alkali treatment on)
IT Alcohols, properties
RL: PRP (Properties)
(sorption and diffusion of, in **chitosan** complex membranes, alkali treatment effect on)
IT **1310-73-2, Sodium hydroxide**, uses and miscellaneous
RL: USES (Uses)
(**chitosan** complex membranes treated with, sorption and diffusion of water and alcs. in)
IT **64-19-7D**, Acetic acid, **chitosan** complexes 7487-88-9D, Magnesium sulfate, **chitosan** complexes 7720-78-7D, Iron sulfate (FeSO4), **chitosan** complexes 7727-43-7D, Barium sulfate, **chitosan** complexes 7758-98-7D, Copper sulfate, **chitosan** complexes 7786-81-4D, Nickel sulfate, **chitosan** complexes **9012-76-4D, Chitosan**, acetic acid or metal complexes 10043-01-3D, Aluminum sulfate, **chitosan** complexes 10124-43-3D,

chitosan complexes
RL: USES (Uses)
(membranes, sorption and diffusion of water and alcs. in, alkali treatment effect on)

IT 64-17-5, Ethanol, properties **67-56-1, Methanol**, properties 67-63-0, Isopropanol, properties 71-23-8, Propanol, properties 7732-18-5, Water, properties
RL: PRP (Properties)
(sorption and diffusion of, in **chitosan** complex membranes, alkali treatment effect on)

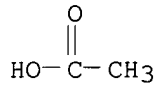
IT **1310-73-2, Sodium hydroxide**, uses and miscellaneous
RL: USES (Uses)
(**chitosan** complex membranes treated with, sorption and diffusion of water and alcs. in)

RN 1310-73-2 HCAPLUS
CN Sodium hydroxide (Na(OH)) (9CI) (CA INDEX NAME)



IT **64-19-7D**, Acetic acid, **chitosan** complexes
9012-76-4D, Chitosan, acetic acid or metal complexes
RL: USES (Uses)
(membranes, sorption and diffusion of water and alcs. in, alkali treatment effect on)

RN 64-19-7 HCAPLUS
CN Acetic acid (7CI, 8CI, 9CI) (CA INDEX NAME)

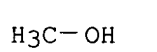


RN 9012-76-4 HCAPLUS
CN Chitosan (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **67-56-1, Methanol**, properties
RL: PRP (Properties)
(sorption and diffusion of, in **chitosan** complex membranes, alkali treatment effect on)

RN 67-56-1 HCAPLUS
CN Methanol (8CI, 9CI) (CA INDEX NAME)



L104 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2002 ACS
AN **1988:77423** HCAPLUS
DN **108:77423**
TI Formation of ordered phases of **hydroxypropyl cellulose** in miscible and immiscible isobutyric acid/**water** mixtures
AU Laivins, G. V.; Sixou, P.
CS Lab. Phys. Matiere Condens., Univ. Nice, Nice, 06034, Fr.
SO Journal of Polymer Science, Part B: Polymer Physics (1988), 26(1), 113-25
CODEN: JPBPEM; ISSN: 0887-6266
DT Journal
LA English

CC 43-3 (Cellulose, Lignin, Paper, and Other Wood Products)

AB **Hydroxypropyl cellulose** (I) is known to form birefringent liq.-cryst. phases at elevated polymer concns. in either **water** or isobutyric acid (II). The I concn. at which the polymeric phase exhibits birefringence decreases as the II content in mixed **H2O**-II **solvents** decreases, even though the concn. .vphi.ci for the formation of an ordered phase of I in **water** is greater than that in II. **Water** is a spectator component and apparently does not participate in the formation of a birefringent phase when II is present. A birefringent phase forms once the concn. of II in the soln. omitting the **H2O** equals the .vphi.ci of binary I-II solns. for temps. from 23 to 95.degree.C. The strong preferential affinity of I for II is visually evident as an I coagulate separates from **dil.** soln. when the **solvent** mixt. contains as little as 5% II. The coagulate dissolves to give a monophasic isotropic soln. as the II content in the **solvent** is increased. A heterogeneous system in which a clear supernatant fluid covers a pearly white polymeric phase forms when the **solvent** mixt. is immiscible and the **HPC** content is less than 50%. At high I content, the classical appearance assocd. with concd. I solns. is seen. The optical and rheol. properties of the heterogeneous systems are compared with those of homogeneous solns. at several I concns.

ST **hydroxypropyl cellulose** phase **solvent** mixt; isobutyric acid **water hydroxypropyl cellulose**

IT Birefringence
(of **hydroxypropyl cellulose** phases in miscible and immiscible mixts. of isobutyric acid and **water**)

IT Chains, chemical
(ordering of, of **hydroxypropyl cellulose**, in miscible and immiscible isobutyric acid-**water** mixts.)

IT **7732-18-5P, Water**, preparation
RL: PREP (Preparation)
(**hydroxypropyl cellulose** in miscible and immiscible mixts. of isobutyric acid and, formation of ordered phases in)

IT **79-31-2**, Isobutyric acid
RL: USES (Uses)
(**hydroxypropyl cellulose** in miscible and immiscible mixts. of **water** and, formation of ordered phases of)

IT **9004-64-2, Hydroxypropyl cellulose**
RL: USES (Uses)
(in miscible and immiscible isobutyric acid-**water** mixts., formation of ordered phases of)

IT **7732-18-5P, Water**, preparation
RL: PREP (Preparation)
(**hydroxypropyl cellulose** in miscible and immiscible mixts. of isobutyric acid and, formation of ordered phases in)

RN 7732-18-5 HCAPLUS

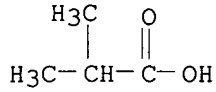
CN Water (8CI, 9CI) (CA INDEX NAME)

H_2O

IT **79-31-2**, Isobutyric acid
RL: USES (Uses)
(**hydroxypropyl cellulose** in miscible and immiscible mixts. of **water** and, formation of ordered phases of)

RN 79-31-2 HCAPLUS

CN Propanoic acid, 2-methyl- (9CI) (CA INDEX NAME)



IT **9004-64-2, Hydroxypropyl cellulose**
RL: USES (Uses)
(in miscible and immiscible isobutyric acid-**water** mixts., formation of ordered phases of)
RN 9004-64-2 HCAPLUS
CN Cellulose, 2-hydroxypropyl ether (9CI) (CA INDEX NAME)

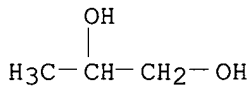
CM 1

CRN 9004-34-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 57-55-6
CMF C3 H8 O2



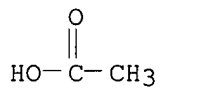
L104 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2002 ACS
AN **1988:62516** HCAPLUS
DN **108:62516**
TI Bandage sheet for the protection of wounds
IN Kibune, Koji; Yamaguchi, Yasuhiko; Motosugi, Kenzo; Tanae, Hiroyuki
PA Unitika Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61L015-01
CC **63-7** (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 62170254	A2	19870727	JP 1986-11424	19860120
JP 05068265	B4	19930928		

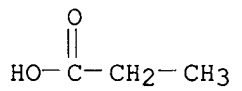
AB A bandage contains a **chitosan** sheet treated with anhyd. AcOH, propionic acid, or anhyd. butyric acid. **Chitin** was pulverized, treated with 40% by wt. **NaOH** soln. at 121.degree. for 2 h, neutralized with HCl, washed with H2O, and dried to give **chitosan**. The **chitosan** was dissolved in 5% by vol. AcOH soln. at 20.degree., and filtered through a 1480-mesh screen. The soln. was deaerated by reduced pressure and extruded from 0.07 mm-diam. holes into 5% **NaOH**, washed with H2O, and dried to obtain filaments. The filaments were cut 8 mm long, soaked in a 2% by vol. anhyd. AcOH-contg. **MeOH** for 1 h, and made into an unwoven sheet. The thickness of the sheet was 0.16 mm.
ST bandage **chitosan** acid treatment
IT Medical goods

(bandages, **chitosan** sheet for, org. acid-treated)
IT Synthetic fibers, polymeric
RL: PREP (Preparation)
(**chitosan**, bandage sheet prepn. from)
IT **1398-61-4, Chitin**
RL: BIOL (Biological study)
(**chitosan** prepn. from, for bandage sheet prepn.)
IT **64-19-7**, Acetic acid, biological studies **79-09-4**, Propionic acid, biological studies **107-92-6**, Butyric acid, biological studies
RL: BIOL (Biological study)
(**chitosan** treatment with, for bandage sheet prepn.)
IT **9012-76-4P, Chitosan**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and acid treatment of, for bandage sheet prepn.)
IT **1398-61-4, Chitin**
RL: BIOL (Biological study)
(**chitosan** prepn. from, for bandage sheet prepn.)
RN 1398-61-4 HCAPLUS
CN Chitin (8CI, 9CI) (CA INDEX NAME)

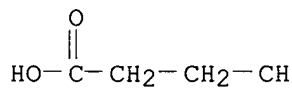
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **64-19-7**, Acetic acid, biological studies **79-09-4**, Propionic acid, biological studies **107-92-6**, Butyric acid, biological studies
RL: BIOL (Biological study)
(**chitosan** treatment with, for bandage sheet prepn.)
RN 64-19-7 HCAPLUS
CN Acetic acid (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 79-09-4 HCAPLUS
CN Propanoic acid (9CI) (CA INDEX NAME)



RN 107-92-6 HCAPLUS
CN Butanoic acid (9CI) (CA INDEX NAME)



IT **9012-76-4P, Chitosan**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and acid treatment of, for bandage sheet prepn.)
RN 9012-76-4 HCAPLUS
CN Chitosan (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

```
=> d his

     (FILE 'HOME' ENTERED AT 11:35:44 ON 29 OCT 2002)
               SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 11:36:23 ON 29 OCT 2002

     FILE 'HCAPLUS' ENTERED AT 11:36:44 ON 29 OCT 2002
               E US2001-330081/AP,PRN
               E HUANG Y/AU
L1          647 S E3,E19
               E HUANG YUN/AU
L2           58 S E3,E20
               E HUANG YUNPENG/AU
               E LEE F/AU
L3          428 S E3-E41
               E LEE FANG/AU
               E SHAW J/AU
L4          173 S E3
               E SHAW JER/AU
               E YUNG/PA,CS
               E EXCIPIENT/CT
               E EXCIPIENT/CW
               E EXCIPIENT
L5         8613 S E2-E8
L6            1 S L1-L4 AND L5
               E POLYSACCHARIDE/CT
               E E13+ALL
L7        36764 S E4,E3
L8            1 S E26,E27
L9       147416 S E39-E42,E44,E45,E50,E51,E58,E64,E65,E66,E71,E73,E92,E98,E99,E

     FILE 'REGISTRY' ENTERED AT 11:44:53 ON 29 OCT 2002
               E GELATIN/CN

     FILE 'HCAPLUS' ENTERED AT 11:44:53 ON 29 OCT 2002

     FILE 'REGISTRY' ENTERED AT 11:44:57 ON 29 OCT 2002

     FILE 'HCAPLUS' ENTERED AT 11:44:57 ON 29 OCT 2002

     FILE 'REGISTRY' ENTERED AT 11:45:00 ON 29 OCT 2002

     FILE 'HCAPLUS' ENTERED AT 11:45:00 ON 29 OCT 2002

     FILE 'REGISTRY' ENTERED AT 11:45:03 ON 29 OCT 2002

     FILE 'HCAPLUS' ENTERED AT 11:45:04 ON 29 OCT 2002

     FILE 'REGISTRY' ENTERED AT 11:45:05 ON 29 OCT 2002

     FILE 'HCAPLUS' ENTERED AT 11:45:05 ON 29 OCT 2002
               E GELATIN/CT
               E E3+ALL
L10         2295 S E1
               E E2+ALL
L11        17377 S E4

     FILE 'REGISTRY' ENTERED AT 11:45:37 ON 29 OCT 2002
L12           14 S 9005-25-8 OR 9004-34-6 OR 1398-61-4 OR 32609-14-6 OR 9000-30-
L13            1 S 9000-01-5
L14           13 S L12 NOT ARABIC
L15           14 S L13,L14
```

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                E CROSCARMELLOSE/CN
                E CHITOSAN/CN
L16           6 S 67-56-1 OR 64-17-5 OR 71-23-8 OR 67-63-0 OR 62309-51-7 OR 67-
L17           1 S WATER/CN

     FILE 'HCAPLUS' ENTERED AT 11:53:11 ON 29 OCT 2002
L18      148918 S L15
L19      557593 S STARCH OR ?CELLULOS? OR CHITIN OR GUM(A)ARABIC OR GUM(A)GUAR
L20        7327 S (HYDROXYPROPYL OR HYDROXYPROPYLMETHYL OR HYDROXY()(PROPYL OR
L21       71726 S POLYSACCHARIDE
L22      617605 S L7-L9,L18-L21
L23        2788 S L5 AND L22
L24      265669 S L16
L25      963617 S METHANOL OR ETHANOL OR PROPANOL OR ISOPROPANOL OR ACETONE OR
L26       54245 S L22 AND L24,L25
L27       37853 S L22 AND SOLVENT
L28        6625 S L26 AND L27 AND (L17 OR H2O OR WATER)
L29          26 S L23 AND L28
L30          19 S L18 AND L29
L31           9 S L24 AND L30
                SEL DN AN 1 7
L32           2 S L31 AND E1-E6
L33          17 S L29 NOT L31
                SEL DN AN 6 12
L34           2 S E7-E12 AND L33
L35           4 S L32,L34
L36       80182 S L26,L27

     FILE 'REGISTRY' ENTERED AT 12:13:31 ON 29 OCT 2002

     FILE 'HCAPLUS' ENTERED AT 12:13:31 ON 29 OCT 2002


     FILE 'HCAPLUS' ENTERED AT 12:16:10 ON 29 OCT 2002
L37       18036 S L36 AND H2O
L38        2107 S L36 AND L17
L39       22786 S L36 AND WATER
L40       36436 S L37-L39

     FILE 'REGISTRY' ENTERED AT 12:17:33 ON 29 OCT 2002

     FILE 'HCAPLUS' ENTERED AT 12:17:33 ON 29 OCT 2002

     FILE 'REGISTRY' ENTERED AT 12:27:38 ON 29 OCT 2002
L41             TRA L40 1- RN :    50908 TERMS

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L42       50395 SEA L41
L43             STR
L44             SCR 2043 OR 2039 OR 2050 OR 2049 OR 2048 OR 2053 OR 2051 OR 205
L45          50 S L43 NOT L44 CSS SAM
L46           2 S L45/COM
L47             STR L43
L48           6 S L47 CSS SAM
L49           3 S (ETHANOIC ACID OR PROPANOIC ACID OR BUTANOIC ACID)/CN
L50         285 S (C3H6O2 OR C4H8O2 OR C5H10O2)/MF NOT (LABELLED OR 11C# OR 13C
L51         717 S (C3H6O2 OR C4H8O2 OR C5H10O2)/MF NOT (LABELED OR 11C# OR 13C#
L52         317 S L51 AND NR>=1
L53         400 S L51 NOT L52
L54         363 S L53 NOT ESTER
L55          23 S L54 AND ACID
L56          12 S L55 NOT ION
L57          13 S L49,L56
```

```
L58           1 S 71-50-1
L59         229 S (C3H5O2 OR C4H7O2 OR C5H11O2)/MF NOT (LABELED OR 11C# OR 13C#
L60          53 S L59 AND NR>=1
L61         176 S L59 NOT L60
L62          35 S L61 AND ION
L63           9 S L62 AND (PROPANOIC OR BUTANOIC)
                SEL RN 1 5 6
L64           6 S L63 NOT E13-E15
L65           7 S L58,L64
L66          20 S L57,L65
                SEL RN
L67       34220 S E16-E35/CRN
L68         608 S L67 AND (CA OR K OR NA)/ELS
L69          99 S L68 AND 2/NC
L70          36 S L69 AND NR>=1
L71          63 S L69 NOT L70
L72          49 S L71 NOT (IDS/CI OR F/ELS OR LYSIN?)
L73          47 S L72 NOT (BR/ELS OR GLYCYL)
L74          67 S L66,L73
L75           2 S (C2H3CAO2 OR C2H3NAO2 OR C2H3KO2)/MF
L76           4 S (C3H5CAO2 OR C3H5NAO2 OR C3H5KO2 OR C4H7CAO2 OR C4H7NAO2 OR C
L77           1 S SODIUM HYDROXIDE/CN
L78          73 S L66,L74-L76

     FILE 'HCAPLUS' ENTERED AT 13:13:32 ON 29 OCT 2002
L79      101308 S L78
L80        1821 S L36 AND L79
L81         180 S L80 AND (L77 OR NAOH OR (NA OR SODIUM)()HYDROXIDE)
L82         773 S L80,L81 AND L40
L83           4 S L82 AND EXCIPIENT
L84          50 S L82 AND DILU?
L85          19 S L82 AND FILL?
L86           1 S L83 AND L84,L85
L87           3 S L83 NOT L86
                SEL DN AN 1
L88           1 S E36-E38 AND L87
L89           4 S L35,L88
L90          68 S L84-L85 NOT L89
                SEL DN AN 30 43
L91           2 S L90 AND E38-E44
L92           6 S L89,L91
L93           6 S L92 AND L1-L11,L18-L40,L79-L92
L94           5 S L93 NOT DAPHNE

     FILE 'REGISTRY' ENTERED AT 13:22:48 ON 29 OCT 2002
L95           1 S METHANOL/CN

     FILE 'HCAPLUS' ENTERED AT 13:23:14 ON 29 OCT 2002
L96        3335 S L95 AND L22
L97       16831 S (MEOH OR METHANOL OR METHYLALC? OR METHYL ALCOHOL) AND L22
L98       17191 S L96,L97
L99         519 S L98 AND L79
L100         72 S L99 AND (L77 OR NAOH OR (NA OR SODIUM)()HYDROXIDE)
L101          0 S L100 AND EXCIPIENT
L102         12 S L100 AND (1 OR 63 OR 33)/SC,SX
                SEL DN AN 2 7 8 10 11
L103          5 S L102 AND E45-E59
L104         10 S L94,L103

     FILE 'HCAPLUS' ENTERED AT 13:27:14 ON 29 OCT 2002

=> fil wpix
FILE 'WPIX' ENTERED AT 13:49:35 ON 29 OCT 2002
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FILE LAST UPDATED: 26 OCT 2002 <20021026/UP>
MOST RECENT DERWENT UPDATE: 200269 <200269/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> SLART (Simultaneous Left and Right Truncation) is now
available in the /ABEX field. An additional search field
/BIX is also provided which comprises both /BI and /ABEX <<<

>>> The BATCH option for structure searches has been
enabled in WPINDEX/WPIDS and WPIX <<<

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http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d all abeq tech abex tot

L134 ANSWER 1 OF 6 WPIX (C) 2002 THOMSON DERWENT
AN **2002-507790** [54] WPIX
DNC **C2002-144303**
TI Fibrous **cellulose excipient** used as binder in
pharmaceuticals used for dermatological disorders, comprises
cellulose lattice with preset bulk density and tap density.
DC A11 A96 B07
IN KUMAR, V
PA (IOWA) UNIV IOWA RES FOUND; (KUMA-I) KUMAR V
CYC 94
PI WO 2002022172 A2 20020321 (200254)* EN 24p A61K047-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001083107 A 20020326 (200254) A61K047-00
US 2002061335 A1 20020523 (200254) A61K009-14
ADT WO 2002022172 A2 WO 2001-US24404 20010803; AU 2001083107 A AU 2001-83107
20010803; US 2002061335 A1 Provisional US 2000-232657P 20000914, US
2001-946658 20010905
FDT AU 2001083107 A Based on WO 200222172
PRAI US 2000-232657P 20000914; US 2001-946658 20010905
IC ICM A61K009-14; A61K047-00
ICS A01N025-12; A61K007-00; C08B001-00
AB WO 200222172 A UPAB: 20020823
NOVELTY - A fibrous **cellulose excipient** (I) comprises
a **cellulose** II lattice with a bulk density of 0.2 - 0.5 g/cm3
and a tap density of 0.4 - 0.7 g/cm3.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
following:
(1) preparation of (I);
(2) preparation of a topical formulation; and
(3) method of making **cellulose** beads for use in controlled

release pharmaceuticals and as immobilizing agents, which involves drying aqueous (I).

USE - (I) Is used in the preparation of food, pharmaceutical and agricultural products, cosmetics and **cellulose** bead (claimed). (I) Is also used as a filler/binder/disintegrant in the design and development of solid compacts and capsules, as a drug carrier or bodying agent in the manufacture of dermatological products, and in the form of **cellulose** beads used as tabletting aids for controlled release products, as immobilizing agents for isolation of nucleic acids and other compounds such as biocides for use in agricultural products, or as an absorbent for oils, flavors and fragrances.

ADVANTAGE - (I) Simplifies the manufacturing procedure by producing pharmaceuticals without the need of a separate disintegrant, and hence decreases manufacturing cost. The resulting tablet disintegrates rapidly in **water** to produce fine particles used to prepare tablets. The superior disintegrating properties of (I) attributes for the higher affinity of (I) to **water** molecules. (I) Can also be readily converted into an aqueous dispersion by mechanical attrition in **water**, with or without the aid of a suspending or viscosity enhancing agent.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: A03-A04A1; A12-V01; **B04-C02A**; B12-M10A; B12-M11B; B12-M11D

TECH UPTX: 20020823

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) is prepared by: (i) soaking and agitating **cellulose** (II) in alkali metal hydroxide for 4 - 12 hours to form a homogeneous gel;
(ii) precipitating with an alcohol;
(iii) filtering;
(iv) washing with **water**;
(v) drying at room temperature or in an oven at 50 - 55 degrees C.
Alternatively, (I) is prepared by soaking **cellulose** fibers (III) in alkali metal hydroxide to form a swollen mass, washing with **water** and reacting with a dilute mineral acid at boiling temperature until a fine powder is formed, which is then filtered, washed with **water** to a neutral pH and precipitated with an alcohol.
Preferred Alcohol: The alcohol is **methanol**, **isopropyl alcohol**, propylene glycol, or preferably **ethanol**.
Preferred Process: During the preparation of topical formulation, a suspending agent is further added to the topical drug or cosmetic.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Hydroxide: The alkali metal hydroxide is aqueous **sodium hydroxide** with concentration of at least 5N.
Preferred Acid: The mineral acid is hydrochloric acid, nitric acid or sulfuric acid.
TECHNOLOGY FOCUS - POLYMERS - Preferred Properties: (I) Has X-ray diffraction patterns at 12, 20, and 22 degrees 2 theta and disintegrates in less than 30 seconds.
Preferred Form: (I) is a dried and partially aggregated fibrous material, present in an aqueous dispersion or in a compressed form.
Preferred Component: (III) is **cellulose** powder, alpha-**cellulose** or hard/soft/purified wood pulp.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Form: The pharmaceutical is a compressed tablet containing 0.5 - 99 weight% of (I).

ABEX

EXAMPLE - 5N Sodium hydroxide solution (300 ml) was slowly added to powder cellulose (50 g) and the resulting paste-like mass was allowed to stand for 12 hours at room temperature after which ethanol (210 ml) was added with vigorous agitation. A fine powder was precipitated, filtered and washed with water to a neutral pH. The wet cake was dried at 50 - 55

degrees C and sieved to different particle size fractions. The powder fractions had particle size of 45 - 104 microm, bulk density of 0.469 g/cc, tap density of 0.509 g/cc and moisture content of at most 5%.

L134 ANSWER 2 OF 6 WPIX (C) 2002 THOMSON DERWENT
AN **2001-265859** [27] WPIX
DNC **C2001-080430**
TI Preparation of stable formulations of angiotensin converting enzyme inhibitors comprising mixing an alcoholic dispersion of the ACE inhibitor with an aqueous metal compound dispersion.
DC A96 B02 B03
IN SPIREAS, S
PA (MUTU-N) MUTUAL PHARM CO INC
CYC 94
PI WO 2001015724 A1 20010308 (200127)* EN 31p A61K038-55
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000070797 A 20010326 (200137) A61K038-55
ADT WO 2001015724 A1 WO 2000-US23539 20000828; AU 2000070797 A AU 2000-70797 20000828
FDT AU 2000070797 A Based on WO 200115724
PRAI US 2000-598200 20000621; US 1999-387419 19990831; US 2000-492584 20000127
IC ICM A61K038-55
ICS A61K009-16; A61K009-20
AB WO 200115724 A UPAB: 20010518
NOVELTY - A new method for preparing stable formulations of angiotensin converting enzyme (ACE) inhibitors comprises mixing an alcoholic dispersion of the ACE inhibitor with an aqueous metal compound dispersion.

DETAILED DESCRIPTION - A novel method of preparing a stable formulation of enalapril maleate (EM) comprises: (a) mixing EM with an alcohol to form an alcoholic dispersion; (b) dispersing or dissolving a metal compound in **water** to form a metal compound dispersion or solution; and (c) mixing the alcoholic dispersion and the metal compound dispersion. INDEPENDENT CLAIMS are also included for:

(1) a method of preparing a stable formulation of ACE inhibitor which comprises: (a) mixing an ACE inhibitor with an alcohol to form an alcoholic dispersion; (b) dispersing or dissolving a metal compound in **water** to form a metal compound dispersion or solution; and (c) mixing the alcoholic dispersion and the metal compound dispersion;

(2) a method of converting an ACE inhibitor into a stabilized ACE inhibitor comprising the initial step of mixing the ACE inhibitor with an alcohol;

(3) a pharmaceutical preparation comprising a stabilized ACE inhibitor free of breakdown products;

(4) a stabilized ACE inhibitor which contains at most 5 wt.% breakdown products of the ACE inhibitor after incubation at 60 deg. C with 75% relative humidity for 10 days;

(5) a method of preparing a stable formulation of quinapril hydrochloride (QHC) comprising: (a) mixing QHC with an alcohol to form an alcoholic dispersion; (b) dispersing or dissolving a metal compound in **water** to form a metal compound dispersion or solution; and (c) mixing the alcoholic dispersion and the metal compound dispersion;

(6) a method of converting QHC into quinapril sodium comprising the initial step of mixing QHC with an alcohol; and

(7) a pharmaceutical preparation comprising quinapril sodium free of breakdown products.

ACTIVITY - Cardiant; Hypotensive.

MECHANISM OF ACTION - ACE inhibitors.

USE - The ACE inhibitors are useful in the treatment of cardiovascular disorders, especially hypertension.

ADVANTAGE - The presence of alcohol not only accelerates the manufacture of the product but also minimizes extensive hydrolysis and/or cyclization of the product during production and storage. The methods can be used to produce stable ACE inhibitor compositions which are free of breakdown products. They can produce compositions which contain at most 1.0% breakdown products by weight of the ACE inhibitor after incubation at 60 deg. C with 75% relative humidity for 10 days.

Dwg.0/4

FS CPI

FA AB; DCN

MC CPI: A12-V01; B04-C03; B05-A01B; B06-D03; B06-D04; B07-D03; B10-E04D; B12-M06; B14-F02B1

TECH UPTX: 20010518

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Drugs: The ACE inhibitor may be e.g. enalapril maleate, quinapril HCl, benazepril HCl, moexipril HCl, lisinopril HCl, ramipril HCl, or indopril HCl.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Method: The metal in the compound is preferably an alkali metal or an alkali earth metal e.g. sodium, calcium or magnesium. The metal compound may be e.g. sodium bicarbonate, **sodium hydroxide** or sodium hydrogen carbonate.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: The alcohol is preferably **ethanol**. The method may further comprise adding an antioxidant and **excipients** to the alcoholic dispersion. The **excipient** and clear solution are preferably blended to form a granulate. The antioxidant may be e.g. butyl hydroxyl anisole, butyl hydroxyl toluene, maleic acid or ascorbic acid. The compositions may further comprise a lubricant e.g. magnesium stearate or glyceryl monostearate.

TECHNOLOGY FOCUS - POLYMERS - Preferred Method: The dispersions are preferably mixed until a clear solution is attained. The method may further comprise adding microcrystalline **cellulose** to the clear solution. The metal compound dispersion may further comprise a thickening agent e.g. polyethylene glycol, propylene glycol, glycerin, crosslinked povidone, **hydroxypropylmethylcellulose** or polyvinyl pyrrolidone. The method may further comprise adding an antioxidant and **excipients** to the alcoholic dispersion. **Excipients** may include a disintegrating agent e.g. **starch**, **cellulose**, sodium **starch** glycolate, crosslinked povidone or modified **cellulose**.

ABEX

ADMINISTRATION - The compositions can be formed into a pharmaceutical dosage form e.g. a tablet, caplet, bead or capsule.

EXAMPLE - Enallapril maleate (20 mg/unit dose (ud)) was suspended in denatured alcohol (50 mg/ud) with stirring at 500 rpm. Full dispersion of the analapril maleate in the alcohol was achieved in less than 10 seconds. In a separate container, sodium bicarbonate (11 mg/ud) and povidone (polyvinyl pyrrolidone) was dissolved in 100 mg/ud purified water (USP). The sodium bicarbonate/povidine solution was added gradually to the alcoholic drug dispersion with constant stirring (200 rpm) until a clear solution was achieved to yield solution 1.

Microcrystalline cellulose (225 mg/ud), sodium starch glycolate (30 mg/ud), and silicon dioxide (8 mg/ud) were mixed for 3 minutes in a high shear mixer for 3 minutes to yield mixture 1.

Mixture 1 was blended with solution 1 for 3 minutes at low speed with the choppers set to low. The resulting granulation was then dried for 12 hours at 50degreesC. The dried granulation was then passed through a 30 micron mesh sieve and blended with magnesium stearate (2 mg/ud), producing the

final tabletting blend. Formulations were stored at 60 degreesC with 75% relative humidity to simulate extended storage. Stability of the formulations was assessed at 5, 10 and 15 days by HPLC. The results showed that the formulation was more stable than the VASOTEC (RTM) formulation at the 5, 10 and 15 day time points.

L134 ANSWER 3 OF 6 WPIX (C) 2002 THOMSON DERWENT
AN **1998-457068** [39] WPIX
DNC **C1998-138233**
TI Manufacture in an aqueous medium of crosslinked **amylose** - is useful as an **excipient** for controlled release of active compounds from tablets or pellets.
DC A11 A96 B07 P42
IN CARRIERE, F; DUMOULIN, Y; INGENITO, A
PA (ROUI) ROUGIER INC; (LABO-N) LABOPHARM INC
CYC 82
PI WO 9835992 A1 19980820 (199839)* EN 35p C08B031-00
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
US 5807575 A 19980915 (199844) A61K009-22
AU 9859785 A 19980908 (199904) C08B031-00
EP 960131 A1 19991201 (200001) EN C08B031-00
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
NZ 337171 A 20000929 (200060) C08B033-00
AU 726272 B 20001102 (200062) C08B031-00
EP 960131 B1 20020116 (200212) EN C08B031-00
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 69803159 E 20020221 (200221) C08B031-00
ES 2171008 T3 20020816 (200265) C08B031-00
ADT WO 9835992 A1 WO 1998-CA106 19980210; US 5807575 A US 1997-800518 19970214; AU 9859785 A AU 1998-59785 19980210; EP 960131 A1 EP 1998-902905 19980210, WO 1998-CA106 19980210; NZ 337171 A NZ 1998-337171 19980210, WO 1998-CA106 19980210; AU 726272 B AU 1998-59785 19980210; EP 960131 B1 EP 1998-902905 19980210, WO 1998-CA106 19980210; DE 69803159 E DE 1998-603159 19980210, EP 1998-902905 19980210, WO 1998-CA106 19980210; ES 2171008 T3 EP 1998-902905 19980210
FDT AU 9859785 A Based on WO 9835992; EP 960131 A1 Based on WO 9835992; NZ 337171 A Based on WO 9835992; AU 726272 B Previous Publ. AU 9859785, Based on WO 9835992; EP 960131 B1 Based on WO 9835992; DE 69803159 E Based on EP 960131, Based on WO 9835992; ES 2171008 T3 Based on EP 960131
PRAI US 1997-800518 19970214
IC ICM A61K009-22; C08B031-00; C08B033-00
ICS A61K009-14; A61K047-36
AB WO 9835992 A UPAB: 19981001
A process for industrial manufacture, in an aqueous medium, of a cross-linked **amylose**, which is a slow release **excipient** for use in the preparation of tablets and pellets, comprises: (a) subjecting a high **amylose starch** (HAS) to gelatinisation; (b) cross-linking the product from (a) with 1-5 g cross-linking agent per 100 g gelatinised **starch** in an alkali medium; (c) neutralising the reaction medium from (b), forming by products (mainly salts) which are removed without using organic solvent, and recovering the cross-linked HAS slurry; (d) heating the slurry at at least 60 deg. C, and (e) drying the product from (d) to give solid particles of cross linked **amylose**.

In step (a), an aqueous dispersion of HAS is treated with **NaOH**, or is thermomechanically treated using a scraped surface heat exchanger. Step (b) is carried out at pH 10-14, at 20-60 deg. C for 0.5-40 hour, with a cross-linking agent selected from trisodium

trimetaphosphate, epichlorhydrin, adipic acetic anhydride and phosphorus oxychloride. In step (c), by-products are removed by an aqueous continuous ultrafiltration. The recovered cross-linked HAS slurry is concentrated in the absence of organic solvent at a concentration of at most 10 wt.% solids, by evaporation under vacuum. Step (d) is carried out at 90 deg. C for about 2 minutes. In step (e), lyophilisation is followed by pulverisation, or spray-drying is followed by wet granulation.

USE - The cross-linked **amylose** is useful in the preparation of controlled release dosage forms by direct compression.

ADVANTAGE - The process is more economical and safer than previous methods using **acetone**.

Dwg.0/0

FS CPI GMPI
FA AB; DCN
MC CPI: A03-A; A08-D01; A10-E01; A11-C02; A12-V01; **B04-C02**; B10-D03; B12-M10

L134 ANSWER 4 OF 6 WPIX (C) 2002 THOMSON DERWENT
AN **1998-401335** [35] WPIX
DNC **C1998-121617**
TI **Starch**-free, **hemicellulose**-rich bran extract preparation - by treatment with **water** and alkali, used e.g. as dietary fibre, thickener or coating agent.
DC A11 B04 C03 D13 D17 D21 F06 F09 G02
IN GASET, A; RAYNAL, R; RIGAL, L; IOUALALEN, R
PA (ARDE-N) ARDEVAL CHAMPAGNE ARDENNE ASSOC LOI 1901; (ARDE-N) ARDEVAL CHAMPAGNE ARDENNE
CYC 20
PI FR 2758332 A1 19980717 (199835)* 19p C08B030-10
WO 9831713 A1 19980723 (199835) FR 24p C08B037-14
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
ADT FR 2758332 A1 FR 1997-372 19970116; WO 9831713 A1 WO 1998-FR83 19980116
PRAI FR 1997-372 19970116
IC ICM C08B030-10; C08B037-14
ICS C08B030-04; C08L001-02; C08L097-02
ICA A23L001-0534; A23L001-308; C09D105-14
ICI C08L005:14, C08L097-02
AB FR 2758332 A UPAB: 19980904
Production of a **starch**-free extract of bran and a **cellulosic** raffinate is as follows. Bran is mixed with 10 times its volume of **water** below 50 deg. C. The mixture is filtered to recover **starch** suspension and bran. The **starch** liquor is decanted, filtered or centrifuged, then the product is dried. This procedure is repeated once or twice until the level of **starch** in the bran is below 1% calculated as dry weight. The bran is then contacted at 20-100 deg. C with 2-12 wt.% aqueous **sodium hydroxide** solution, at a liquid/solid ratio of 5-100. After 5-120 minutes the mixture is diluted with **water** (if necessary) to give a liquid/solid ratio of at least 25. The residue is separated by filtration or centrifugation. The filtrate is concentrated, acidified to pH 4.5-7 and treated with 2-4 volumes of **ethanol**. The obtained coagulate is dried to give an extract rich in **hemicellulose** (HC). Also claimed is a material (I) obtained by mixing the solid (**cellulosic**) residue obtained during the process, in a proportion of 10-50 wt.%, with readily accessible activated **cellulosic** fibre obtained by fractionating wheat or barley straw. (I) may be thermoformed without the addition of adhesives or other additives.

USE - HC is useful as dietary fibre for controlling cholesterol levels and blood pressure. HC also has numerous other uses, e.g. as **excipient**, flavouring agent or emulsifier in the pharmaceutical, cosmetic and animal feed fields. The present HC-containing extracts have rheological and film-forming properties making them useful as thickening

or gelling additives or coating agents, e.g. as a rheological agent in an acrylic emulsion paint. The **cellulosic** raffinate is useful to form (I), which can be thermoformed to give recyclable, compostable mouldings useful in storage and packaging as a replacement for plastics mouldings. The **starch**-containing by-products are also useful e.g. in the textile, paper and adhesive fields.

ADVANTAGE - The process involves less stages than the conventional treatment, with reduced use of solvents. The HC-rich extract is obtained in high yield and at low cost, and has valuable rheological and film-forming properties.

Dwg.0/0

FS CPI
FA AB
MC CPI: A03-A00A; A10-A; A12-V01; **B04-C02A**; B14-D02A2; B14-F02B; **B04-C02A**; C04-C02A; B14-D02A2; C14-D02A2; B14-F02B; C14-F02B; C04-C02A; C14-D02A2; C14-F02B; D03-G01; D03-H01J; D03-H01T1; D06-H01; D08-B; F05-A06; G02-A05

L134 ANSWER 5 OF 6 WPIX (C) 2002 THOMSON DERWENT
AN **1996-240507** [25] WPIX
DNC **C1996-076824**
TI Oral multiple emulsion preconcentrate - contg. cyclosporin, solvents, surfactant and vitamin-E deriv..
DC A96 B04
IN BALAZS, Z; ERDOEHATI, E; HEIM, C; JANCSO, S; JARABIN, M; JUSZTIN, M; KANYA, K I; KISS, I; KOVACS, I; TAKACS, E; VARGA, Z; KANYA, I; JANESO, S; KORCSMAROS, I; KANYA KORCSMAROS, I; KORCSMAROS, I K; ERDOHATI, E; JUSZTIN, I; KORCSMAROSNE, K
PA (BIOG) BIOGAL GYOEGYSZERGYAR RT; (KOVA-I) KOVACS I; (BIOG) BIOGAL GYOGYSZERGYAR; (BIOG) BIOGAL GYOGYSZERGYAR RT
CYC 20
PI

EP 712631	A2	19960522	(199625)*	EN	10p	A61K038-13
R: AT BE CH DE DK ES FR GB GR IE IT LI NL PT SE						
GB 2295546	A	19960605	(199626)		21p	A61K038-13
DE 19543271	A1	19960605	(199628)		10p	A61K038-13
CZ 9501054	A3	19960717	(199637)			A61K038-13
CA 2145242	A	19960522	(199638)			A61K038-13
US 5583105	A	19961210	(199704)		7p	A61K009-113
EP 712631	A3	19961204	(199707)			A61K038-13
SK 9500544	A3	19970205	(199715)			A61K009-113
GB 2295546	B	19980722	(199831)			A61K038-13
IT 1281337	B	19980218	(199912)			A61K000-00
HU 215966	A	19990728	(199936)			A61K038-13
CZ 286686	B6	20000614	(200037)			A61K038-13
CA 2145242	C	20010807	(200148)	EN		A61K038-13
AT 9501893	A	20010915	(200159)			A61K038-13
AT 408945	B	20020315	(200229)			A61K038-13

ADT EP 712631 A2 EP 1995-106655 19950503; GB 2295546 A GB 1995-23295 19951114; DE 19543271 A1 DE 1995-19543271 19951120; CZ 9501054 A3 CZ 1995-1054 19950425; CA 2145242 A CA 1995-2145242 19950321; US 5583105 A US 1995-414496 19950331; EP 712631 A3 EP 1995-106655 19950503; SK 9500544 A3 SK 1995-544 19950427; GB 2295546 B GB 1995-23295 19951114; IT 1281337 B IT 1995-MI2411 19951121; HU 215966 A HU 1994-3328 19941121; CZ 286686 B6 CZ 1995-1054 19950425; CA 2145242 C CA 1995-2145242 19950321; AT 9501893 A AT 1995-1893 19951121; AT 408945 B AT 1995-1893 19951121
FDT CZ 286686 B6 Previous Publ. CZ 9501054; AT 408945 B Previous Publ. AT 9501893
PRAI HU 1994-3328 19941121
REP 3.Jnl.Ref; DE 3930928; EP 589843; FR 2636534; WO 9511039
IC ICM A61K000-00; A61K009-113
ICS A61K009-107; A61K009-66; A61K031-355; A61K047-10; A61K047-14; A61K047-36; A61P029-00; A61P031-10; A61P033-00; A61P037-00
ICA A61K038-13

ICI A61K031:355; A61K031:355
AB EP 712631 A UPAB: 19960625
Oral multiple emulsion pre-concentrate comprises: (a) 5-30 wt.% cyclosporin, (b) 5-30 wt.% tocopheryl polyethylene glycol carboxylic acid ester, (c) 5-20 wt.% **EtOH**, (d) 20-55 wt.% lipophilic solvent and/or 10-55 wt.% amphiphilic solvent, and (e) opt. 10-20 wt.% co-tenside.
USE - Cyclic poly N-methylated undeca-peptides belonging to the cyclosporin family are immunosuppressive, antiinflammatory, anti-fungal and anti-parasitic agents. Cyclosporin A is used to prevent rejection of organ transplants and for treating serious chronic autoimmune diseases e.g. lupus erythematosus, glomerulonephritis, haemolytic anaemia, myasthenia gravis and multiple sclerosis. Vitamin E influences prostaglandin formation by inhibiting arachidonic acid release and enzyme activity of lipoxygenase and inhibits thrombocyte aggregation.
ADVANTAGE - The absorption of cyclosporin is improved over prior art. The compsns. have an oral bioavailability of over 40-48% for cyclosporin. The ingredients do not ppte. during storage at 5-15deg.C and the shelf-life of the compsn. is improved over prior art. Decreasing the ratio of surfactant reduces high dispersivity grade of the emulsion. Vitamin E decreases the nephrotoxic effect of cyclosporins and is more favourable than fish oil contg. omega-3-unsatd. fatty acids because its compsn. is determined and constant.
Dwg.0/2
FS CPI
FA AB; DCN
MC CPI: A10-E07; A10-E08; A12-V01; B02-C; B03-H; B04-C03C; B14-D05C; B14-F04; B14-G02; B14-L08; B14-S01
ABEQ US 5583105 A UPAB: 19970122
An oral multiple emulsion pre-concentrate compsn. comprises (i) cyclosporin, (ii) **ethanol**, (iii) a lipophilic or amphiphilic solvent, (iv) tocopheryl polyethylene (glycol) carboxylic acid ester (as surfactant), and (v) a co-tenside.
USE - Cyclosporin A is used to prevent the rejection of organ transplants and to treat serious chronic autoimmune diseases.
ADVANTAGE - The compsn. has higher bioavailability than the 40-48% bioavailability of known compsns., without requiring bile salts (i.e. in cases of hepatic dysfunction). The tocopheryl component acts as an effective antioxidant, and the surfactants have HLB sufficiently high to solubilise the antioxidant. Active ingredients and **excipients** do not precipitate during storage in a cool place (5-15 deg.C.), so shelf-life is prolonged. The **excipients** are chemically stable, and do not become oxidised or rancid. The compsn. may be added to drinks e.g. **water**, tea, fruit juice or milk, or enclosed in a **gelatin** capsule.
Dwg.0/2

L134 ANSWER 6 OF 6 WPIX (C) 2002 THOMSON DERWENT
AN **1994-293951** [36] WPIX
DNC **C1994-133949**
TI Prepn. of pharmaceutical compsn. free from organic solvent - comprises replacing **water** lost during drying, during blending in a solids processor, to improve stability of active drug.
DC A96 B07
IN DALONZO, G; GALA, P B; SHAH, J J; WEISS, J; D'ALONZO, G
PA (WARN) WARNER LAMBERT CO
CYC 6
PI WO 9418951 A1 19940901 (199436)* EN 17p A61K009-14
RW: OA
W: AU CA JP NZ
AU 9462291 A 19940914 (199502) A61K009-14
US 5478571 A 19951226 (199606) 4p A61K009-14
NZ 262562 A 19960426 (199622) A61J003-02
AU 671536 B 19960829 (199643) A61K009-14

JP 08506831 W 19960723 (199650) 13p A61K009-14
ADT WO 9418951 A1 WO 1994-US381 19940111; AU 9462291 A AU 1994-62291 19940111; US 5478571 A Cont of US 1993-21428 19930223, US 1995-375077 19950117; NZ 262562 A NZ 1994-262562 19940111, WO 1994-US381 19940111; AU 671536 B AU 1994-62291 19940111; JP 08506831 W JP 1994-518960 19940111, WO 1994-US381 19940111
FDT AU 9462291 A Based on WO 9418951; NZ 262562 A Based on WO 9418951; AU 671536 B Previous Publ. AU 9462291, Based on WO 9418951; JP 08506831 W Based on WO 9418951
PRAI US 1993-21428 19930223; US 1995-375077 19950117
REP 01Jnl.Ref; EP 287488
IC ICM A61J003-02; A61K009-14
ICS A61K009-20; A61K009-48; A61K031-56
AB WO 9418951 A UPAB: 19941102
Prepn. of a solid pharmaceutical compsn. which is substantially free of any residual organic solvent comprises: (a) solubilising the active drug in an organic solvent; (b) mixing the drug with at least one inert carrier material; (c) removing solvent and adding a set amt. of **water** when solvent has been reduced to less than half of its original amt.; and (d) removing remaining solvent.

The organic solvent is pref. **EtOH** or **MeOH**. The drug is hormonal, e.g. norethindrone acetate or ethynyl estradiol. The carrier material is lactose, microcrystalline **cellulose**, corn **starch**, dicalcium phosphate, tricalcium phosphate, carboxymethyl **cellulose** sodium, hydroxypropyl methyl **cellulose**, hydroxypropyl **cellulose**, MgCO3, Na2CO3, CaCO3, sugar, sorbitol or gelatinised **starch**. In step (c) 0.1-5.0% **water** is added to the mixt. when the organic solvent is reduced from 50-90% of its original amt.

USE - The presence of residual alcohol in dried pharmaceutical compsns. adversely affects many drugs which must be initially dissolved in alcohol to achieve uniform distribution throughout the **excipient** carrier materials. The process achieves removal of solvent, improving stability of the active drug, and is partic. useful when the drug is formulated in a low strength dosage form.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: A12-V01; B01-A02; B01-C04; B01-C05; **B04-C02A2**; B04-C02B2; B05-A01B; B05-B02A3; B05-C04; B07-A02; B10-E04D
ABEQ US 5478571 A UPAB: 19960212
Method for the preparation of a solid pharmaceutical composition that is substantially free of any residual organic solvent comprising: a) solubilizing an active drug in an organic solvent; b) mixing the drug solution with at least one inert carrier material; c) removing said solvent from said drug carrier blend and adding **water** in the range from about 0.1% to approximately 5.0% based on the total weight of the composition to said blend when said solvent is reduced to less then half of its original amount, and; d) removing the remaining residual solvent to yield a dry powdered active which can be then tabletted or encapsulated.
Dwg.0/0

=> d his

(FILE 'HOME' ENTERED AT 11:35:44 ON 29 OCT 2002)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 11:36:23 ON 29 OCT 2002

FILE 'HCAPLUS' ENTERED AT 11:36:44 ON 29 OCT 2002
E US2001-330081/AP,PRN

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                E HUANG Y/AU
L1          647 S E3,E19
                E HUANG YUN/AU
L2           58 S E3,E20
                E HUANG YUNPENG/AU
                E LEE F/AU
L3          428 S E3-E41
                E LEE FANG/AU
                E SHAW J/AU
L4          173 S E3
                E SHAW JER/AU
                E YUNG/PA,CS
                E EXCIPIENT/CT
                E EXCIPIENT/CW
                E EXCIPIENT
L5         8613 S E2-E8
L6            1 S L1-L4 AND L5
                E POLYSACCHARIDE/CT
                E E13+ALL
L7        36764 S E4,E3
L8            1 S E26,E27
L9       147416 S E39-E42,E44,E45,E50,E51,E58,E64,E65,E66,E71,E73,E92,E98,E99,E

     FILE 'REGISTRY' ENTERED AT 11:44:53 ON 29 OCT 2002
                E GELATIN/CN

     FILE 'HCAPLUS' ENTERED AT 11:44:53 ON 29 OCT 2002

     FILE 'REGISTRY' ENTERED AT 11:44:57 ON 29 OCT 2002

     FILE 'HCAPLUS' ENTERED AT 11:44:57 ON 29 OCT 2002

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     FILE 'REGISTRY' ENTERED AT 11:45:05 ON 29 OCT 2002

     FILE 'HCAPLUS' ENTERED AT 11:45:05 ON 29 OCT 2002
                E GELATIN/CT
                E E3+ALL
L10         2295 S E1
                E E2+ALL
L11        17377 S E4

     FILE 'REGISTRY' ENTERED AT 11:45:37 ON 29 OCT 2002
L12           14 S 9005-25-8 OR 9004-34-6 OR 1398-61-4 OR 32609-14-6 OR 9000-30-
L13            1 S 9000-01-5
L14           13 S L12 NOT ARABIC
L15           14 S L13,L14
                E CROSCARMELLOSE/CN
                E CHITOSAN/CN
L16            6 S 67-56-1 OR 64-17-5 OR 71-23-8 OR 67-63-0 OR 62309-51-7 OR 67-
L17            1 S WATER/CN

     FILE 'HCAPLUS' ENTERED AT 11:53:11 ON 29 OCT 2002
L18       148918 S L15
L19       557593 S STARCH OR ?CELLULOS? OR CHITIN OR GUM(A)ARABIC OR GUM(A)GUAR
L20         7327 S (HYDROXYPROPYL OR HYDROXYPROPYLMETHYL OR HYDROXY()(PROPYL OR
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L21       71726 S POLYSACCHARIDE
L22      617605 S L7-L9,L18-L21
L23        2788 S L5 AND L22
L24      265669 S L16
L25      963617 S METHANOL OR ETHANOL OR PROPANOL OR ISOPROPANOL OR ACETONE OR
L26       54245 S L22 AND L24,L25
L27       37853 S L22 AND SOLVENT
L28        6625 S L26 AND L27 AND (L17 OR H2O OR WATER)
L29          26 S L23 AND L28
L30          19 S L18 AND L29
L31           9 S L24 AND L30
                 SEL DN AN 1 7
L32           2 S L31 AND E1-E6
L33          17 S L29 NOT L31
                 SEL DN AN 6 12
L34           2 S E7-E12 AND L33
L35           4 S L32,L34
L36       80182 S L26,L27

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     FILE 'HCAPLUS' ENTERED AT 12:13:31 ON 29 OCT 2002


     FILE 'HCAPLUS' ENTERED AT 12:16:10 ON 29 OCT 2002
L37       18036 S L36 AND H2O
L38        2107 S L36 AND L17
L39       22786 S L36 AND WATER
L40       36436 S L37-L39

     FILE 'REGISTRY' ENTERED AT 12:17:33 ON 29 OCT 2002

     FILE 'HCAPLUS' ENTERED AT 12:17:33 ON 29 OCT 2002

     FILE 'REGISTRY' ENTERED AT 12:27:38 ON 29 OCT 2002
L41             TRA L40 1- RN :    50908 TERMS

     FILE 'REGISTRY, REGISTRY' ENTERED AT 12:27:38 ON 29 OCT 2002
L42       50395 SEA L41
L43             STR
L44             SCR 2043 OR 2039 OR 2050 OR 2049 OR 2048 OR 2053 OR 2051 OR 205
L45          50 S L43 NOT L44 CSS SAM
L46           2 S L45/COM
L47             STR L43
L48           6 S L47 CSS SAM
L49           3 S (ETHANOIC ACID OR PROPANOIC ACID OR BUTANOIC ACID)/CN
L50         285 S (C3H6O2 OR C4H8O2 OR C5H10O2)/MF NOT (LABELLED OR 11C# OR 13C
L51         717 S (C3H6O2 OR C4H8O2 OR C5H10O2)/MF NOT (LABELED OR 11C# OR 13C#
L52         317 S L51 AND NR>=1
L53         400 S L51 NOT L52
L54         363 S L53 NOT ESTER
L55          23 S L54 AND ACID
L56          12 S L55 NOT ION
L57          13 S L49,L56
L58           1 S 71-50-1
L59         229 S (C3H5O2 OR C4H7O2 OR C5H11O2)/MF NOT (LABELED OR 11C# OR 13C#
L60          53 S L59 AND NR>=1
L61         176 S L59 NOT L60
L62          35 S L61 AND ION
L63           9 S L62 AND (PROPANOIC OR BUTANOIC)
                 SEL RN 1 5 6
L64           6 S L63 NOT E13-E15
L65           7 S L58,L64
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L66          20 S L57,L65
                SEL RN
L67       34220 S E16-E35/CRN
L68         608 S L67 AND (CA OR K OR NA)/ELS
L69          99 S L68 AND 2/NC
L70          36 S L69 AND NR>=1
L71          63 S L69 NOT L70
L72          49 S L71 NOT (IDS/CI OR F/ELS OR LYSIN?)
L73          47 S L72 NOT (BR/ELS OR GLYCYL)
L74          67 S L66,L73
L75           2 S (C2H3CAO2 OR C2H3NAO2 OR C2H3KO2)/MF
L76           4 S (C3H5CAO2 OR C3H5NAO2 OR C3H5KO2 OR C4H7CAO2 OR C4H7NAO2 OR C
L77           1 S SODIUM HYDROXIDE/CN
L78          73 S L66,L74-L76

     FILE 'HCAPLUS' ENTERED AT 13:13:32 ON 29 OCT 2002
L79      101308 S L78
L80        1821 S L36 AND L79
L81         180 S L80 AND (L77 OR NAOH OR (NA OR SODIUM)()HYDROXIDE)
L82         773 S L80,L81 AND L40
L83           4 S L82 AND EXCIPIENT
L84          50 S L82 AND DILU?
L85          19 S L82 AND FILL?
L86           1 S L83 AND L84,L85
L87           3 S L83 NOT L86
                SEL DN AN 1
L88           1 S E36-E38 AND L87
L89           4 S L35,L88
L90          68 S L84-L85 NOT L89
                SEL DN AN 30 43
L91           2 S L90 AND E38-E44
L92           6 S L89,L91
L93           6 S L92 AND L1-L11,L18-L40,L79-L92
L94           5 S L93 NOT DAPHNE

     FILE 'REGISTRY' ENTERED AT 13:22:48 ON 29 OCT 2002
L95           1 S METHANOL/CN

     FILE 'HCAPLUS' ENTERED AT 13:23:14 ON 29 OCT 2002
L96        3335 S L95 AND L22
L97       16831 S (MEOH OR METHANOL OR METHYLALC? OR METHYL ALCOHOL) AND L22
L98       17191 S L96,L97
L99         519 S L98 AND L79
L100         72 S L99 AND (L77 OR NAOH OR (NA OR SODIUM)()HYDROXIDE)
L101          0 S L100 AND EXCIPIENT
L102         12 S L100 AND (1 OR 63 OR 33)/SC,SX
                SEL DN AN 2 7 8 10 11
L103          5 S L102 AND E45-E59
L104         10 S L94,L103

     FILE 'HCAPLUS' ENTERED AT 13:27:14 ON 29 OCT 2002

     FILE 'WPIX' ENTERED AT 13:28:05 ON 29 OCT 2002
                E EXCIP
L105       6056 S E4-E14,E19,E20
L106        693 S L105 AND ((V751 OR V711 OR V712 OR V713 OR V714 OR V735)/MO,M
L107        911 S L105 AND (B04-C02 OR C04-C02 OR B04-C02A# OR B04-C02A# OR B04
L108        648 S L105 AND ((1863 OR 1852 OR 1835)/DRN OR (R01863 OR R01852 OR
L109       1252 S L106-L108
L110       1407 S L105 AND (STARCH OR ?CELLULOS? OR CHITIN OR GUM(A)(ARABIC OR
L111        390 S L105 AND ?SACCHARIDE?
L112       1936 S L109,L110,L111
L113         58 S (0270 OR 0245 OR 0302 OR 0271 OR 0272)/DRN AND L112
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L114         25 S (R00270 OR R00245 OR R00302 OR R00271 OR R00272)/DCN AND L112
L115        157 S (METHANOL OR ETHANOL OR PROPANOL OR ISOPROPANOL OR ACETONE) A
L116         13 S (METHYL OR ETHYL OR PROPYL OR ISOPROPYL)()ALCOHOL AND L112
L117         43 S (MEOH OR ETOH OR PROH OR IPROH) AND L112
L118        223 S L113-L117
L119          8 S L118 AND (NAOH OR (SODIUM OR NA)()HYDROXIDE)
                E SODIUM HYDROXIDE/DCN
                E E3_ALL
                E SODIUM HYDROXIDE/DCN
                E E3+ALL
L120          5 S L118 AND (E2 OR 1514/DRN)
L121         11 S L119,L120
L122        137 S L118 AND (H2O OR WATER)
L123          4 S L117 AND (1740/DRN OR R01740/DCN)
L124        137 S L122,L123
L125          7 S L124 AND L121
                SEL DN AN 1-3
L126          3 S L125 AND E1-E6
L127          4 S L121 NOT L125
                SEL DN AN 2
L128          1 S L127 AND E7-E8
L129          4 S L126,L128
L130          8 S L124 AND R308/M0,M1,M2,M3,M4,M5,M6
L131          5 S Q615/M0,M1,M2,M3,M4,M5,M6 AND L124
L132          4 S L131 NOT L130
                SEL DN AN 2 3
L133          2 S L132 AND E9-E12
L134          6 S L129,L133

     FILE 'WPIX' ENTERED AT 13:49:35 ON 29 OCT 2002
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